EXHIBIT G

Indirect Methods to Estimate Prevalence

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1. OVERVIEW

The first point to be made is that there are very good reasons to estimate the prevalence of problem drug use—which in this chapter refers almost exclusively to injecting drug use, heroin/opiate, and crack-cocaine use. The second is that population or general household surveys, which usually represent the best direct method of prevalence estimation, are not the answer for estimating these forms of problem drug use. Injecting drug users and opiate/ crack-cocaine users are comparatively rare and a largely "hidden" population—that is, they are hard to access by the usual means and are not readily accessed through surveys or administrative records. Counting the number of problem drug users in contact with treatment, police or other services is not sufficient as a prevalence estimate, since only a proportion of the target population is in contact with these services at any time and there is no available base or denominator.

Indirect methods offer an alternative way of estimating prevalence; some of these have been borrowed from animal ecology and some also are in use for other public health problems. In general indirect methods utilize routinely collected data sources. The discussion below presents examples of their use for estimating the prevalence of injecting drug use. The key to improving the evidence on the prevalence of problem drug use centers on improving the routine collection and integration of data on problem drug users that have as a goal "prevalence estimation".

1.1. Why Estimate Prevalence?

There is a growing recognition that policy-makers require evidence on the national and local prevalence of the problem. Gone are the days when, in response to one of the earliest attempts to estimate the prevalence of heroin use in the United States, a reviewer commented, "why bother estimating incidence and prevalence—would policy be any different if [there were] 300,000 or 3 million". (Hunt, 1974; Rittenhouse et al. 1997). Though some doubt whether policy is sufficiently evidence based, the growth in manuals on how to estimate prevalence and examples of prevalence estimates in support of policy is testament to the interest and importance of providing good evidence on prevalence (See, for example, Hser et al., 1992; GAP, 2002; EMCDDA, 1997, 2000; Hickman et al., 2003; Maxwell, 2000).

Prevalence estimates are required primarily in three key areas, service planning and resource allocation, monitoring key targets, and public health surveil-lance/epidemiology.

1.1.1. Service Planning and Resource Allocation

The prevalence of a disease can be central to arguments for securing resources for an appropriate response in terms of treatment and other measures to reduce

the associated harm. While it is the consequent public health and social problems associated with drug use that are directly or indirectly addressed, it is the overall level of prevalence that is frequently highlighted as a summary measure of these problems.

1.1.2. Monitoring Key Targets

The prevalence of problem drug use is often a component of local or national measures of the "coverage" of treatment or harm reduction. For example, in the United Kingdom the government is monitoring the proportion of problem drug users in contact with treatment. Globally, countries have been asked to estimate and monitor the proportion of injecting drug users in contact with services that seek to prevent Human Immunodeficiency Virus (HIV) infection.

1.1.3. Public Health Surveillance/Epidemiology

Prevalence estimates assist the interpretation and measurement of harms associated with drug use. The burden of HIV, Hepatitis C Virus, fatal overdose, and drug related crime associated with drug use in the population as a whole is related both to the level of risk behaviors found among problem drug users and to the prevalence of problem drug use itself. For example, the attributable risk fraction of mortality that may be caused by injecting/opiate use on adult mortality can be estimated by combining information on the prevalence of injecting/opiate use in the population and the Standardized Mortality Ratio of drug related mortality compared to the general population. (Bargagli et al., forthcoming)

Traditionally, the prevalence of an important public health problem would be one of the outputs of a public health surveillance system. The most common modern definition of "public health surveillance" is "the ongoing systematic collection, analysis, and interpretation of data on specific health events for use in the planning, implementation, and evaluation of public health programs" (CDC, 1988); often paraphrased as "information for action". (CDC, 1992). Public health surveillance systems for many infectious diseases are well established, and in developing countries have been extended to chronic diseases. Drug addiction was mentioned as a likely candidate for surveillance in 1968 (Berkelman and Buehler, 1991) though little work has been done to outline what a surveillance system for "drug addiction" would entail. We will come back to the principles of public health surveillance in the concluding section.

1.2. Why Indirect and Not Direct?

Direct methods for estimating levels of any behavior in a population (e.g. population or household surveys) are often considered a 'gold standard' for measuring prevalence, and they can be very effective in monitoring common drug

using behaviors such as tobacco or alcohol. However, direct methods are inefficient and ineffective when measuring the prevalence of rare, more covert, more stigmatized and more problematic forms of drug use, such as injecting or heroin or crack-cocaine use (NRC, 2001). Therefore there are multiple opportunities for bias. For instance, injecting drug users (IDU) or crack-cocaine users are less likely than non-problematic drug users to live in households included in general household surveys; IDU/crack users may be less likely to participate in the survey even if asked; and injection or crack use may be less likely to be reported than other forms of drug use.

Two studies illustrate these points. First, an analysis of combined surveys of over 90,000 subjects in the United States which presented cases by year of initiation failed to detect any change in the incidence of heroin use between 1960 and 1990—which is highly unlikely to be an accurate picture of use over that time period. (Gfroerer and Brodsky, 1992). Second, the 2001 British Crime Survey, with a sample size of over 30,000 found less than 50 people reporting that they used heroin in the last month, giving an estimate for Britain of 33,000, which is implausible as it falls short of the number of heroin users presenting to treatment sites (Aust et al., 2002).

Equally ineffective is an alternative strategy of compiling a register of known injecting drug users or crack-cocaine users. This is a common response in the monitoring of several diseases such as cancers, AIDS, Congenital Heart Defect, other congenital disorders, and childhood diabetes, but such an approach even if it combined multiple data sources would substantially under-estimate the prevalence of problem drug use. In theory, it is possible to ascertain a complete reporting of all diagnosed cases of diabetes or AIDS. However, in any one year a substantial proportion of problem drug users will not be in contact with any service so that a contact report could be made. In fact, it is not known what proportion of users over their injecting life-course will not have any contact with services.

2. INDIRECT ESTIMATION METHODS

The rationale for indirect estimation methods is that direct methods are impracticable or unreliable, and a simple count of known cases or instances will not suffice. In the absence of a ready-made sampling frame that covers problem drug users (PDU), the classical starting-point for direct methods, investigators turn to other means (Suzman et al., 1988). Animal ecologists face the same problem wanting to know the number or abundance of a specific animal in an area. As a result a number of indirect methods, appropriate to different animals and habitats, have been developed in ecology (Seber, 1982). The parallels between animal ecologists and epidemiologists (both estimating "elusive" and "hidden" populations) seems ready-made for injecting drug use and often have been noted, especially given

Table 1. Potential Data Sources for Indirect Estimation Methods

Data Source	Example
Specialist drug treatment	Drug users on methadone, attending treatment agencies, or in residential care
Low threshold drug agencies	Drug users attending drop-in sites or contacted by out-reach workers
Needle exchange	Drug users registered at needle exchange program (SEP)
Casualty	Drug users attending casualty because of an overdose or other problem
Laboratory	Drug users tested for HIV, HCV or HBV
Police/Prison	Drug users arrested or imprisoned for drug offences, Drug user arrested or imprisoned for other crimes but screened for drug problems
Probation	Drug users on probation
Social services—assessments	Drug users assessed by local social services
Hostels for drug users	Drug users living in hostels
Addict Registers	Drug users reported to a central register
Overdose deaths	Number of deaths due to opiate overdose

the widespread use of capture-recapture methods. However, we caution against reading too much into the parallel, since normally the conduct of the studies and the statistical models are very different.

The starting point for indirect estimation is having data on a sample of problem drug users (referred to as the observed data set), which though may be partial provides some information on the characteristics and number of problem drug users. The aim of the indirect estimation methods is to analyze the observed data set or combine it with other information to estimate the "proportion of the [problem drug use] target population sampled within the observed data set", and thereby to arrive at an estimate of the prevalence. Table 1 shows some potential data sources used in prevalence estimation, some of which may be available locally or could be generated.

Indirect methods use these data sources as their raw material and seek to estimate the sampling intensity, i.e. the proportion of the total number of problem drug users sampled in the study. Often this requires having sufficient information on the data sources to match against subjects who appear on two or more data sources; or to obtain other information on how a specific data source (in Table 1) relates to the overall population of problem drug users. The question of this approach then is whether multiple data sources or samples can be used to ascertain the proportion of subjects observed or not observed at a particular source. In this problem of 'incomplete ascertainment' over multiple data sources, it is important to explicitly recognize that many subjects (problem drug users) are unknown to any one or all of the data sources. The disadvantage of indirect methods is that a series of assumptions are made regarding the relationship of the observed data

set(s) to the numbers of problem drug users in the target population (these are summarized below). Furthermore, violation of the assumptions may lead to bias so that the precision of the estimates or how accurately the model represents the target population cannot be empirically tested. Table 2 summarizes a number of indirect estimation methods.

Therefore the central problem in designing indirect estimation studies is obtaining a random sample of problem drug users in first instance. While it is relatively easy in direct estimation methods to check that a sample has been drawn from the sampling frame in a random manner, at least in so far as the design has been properly operationalized, it is far more difficult to make a similar assessment when using indirect methods. A range of assumptions is required that in essence ensure two things: firstly, that the sample behaves, in statistical terms, as though drawn from a conceptual (but unattainable) sampling frame; and secondly, that the required design procedures are operationally valid (i.e., correctly identifies the sample and its relationship with the total population).

These assumptions (some or all of which apply to the various indirect methods) include the following: having a stable population, having equal probabilities that a single subject will be observed in a given data source, matching of subject characteristics can be made across data sources, and that appearing on a data source is independent of appearing on others.

- 1. Stability of Population: The number of drug users entering or exiting from the population over the period of study is negligible in practical terms. Technically, if the 'time spent at risk of being observed' is known, then corrections can be made to allow for a shifting population—but in practice, this is never the case.
- 2. Equi-probable sampling: There is an equal probability of any subject being observed at a given data source. Technically, where multiple data sources are used, this requirement need apply only to one of the sources.
- 3. Matching definitions: Definitions of groups of subjects and the identification of individual subjects should match correctly across data sources. Technically, this implies no misclassification of subjects as IDU or PDU, or false negative or positive matches of subjects between data sources.
- 4. Source conditional independence: If a subject appears on one data source he/she is not more or less likely to appear on another data source, i.e., positive or negative dependence. Technically, in ecology studies it refers to trap fascination or trap avoidance, or significant interactions in statistical parlance. In theory dependence can be adjusted for in the analysis, except if in a study of n data sources where there are n-way interactions. For example, with two samples the data sources must be independent, with three data sources there must be no 3-way interaction and so on.

In practice, all the methods presume that the data sources are broadly representative of the population being studied, or at least aim for that as the safest design. It has been noted (Cormack, 1992) that in contrast to direct estimation there

Table 2. Indirect Methods of Estimating Prevalence of Injection/Problem Drug Use (IDU/PDU)

Method	Summary	Example
Multiplier methods	Combines data on number of known IDU (benchmark, eg, number in treatment, tested for HIV, fatal OD) and information on proportion of IDU that would appear on benchmark (multiplier, e.g proportion in treatment, tested for HIV, died of fatal OD) to estimate total IDU population.	See Archibald (2001) Hartnoll (1985)
Capture-recapture methods	Takes and matches 3 or more data sources of IDU (eg. Treatment, arrest, syringe exchange), analyses the overlap between the data sources using log-linear models to estimate the number of IDU "unobserved" by the data sets and the total number of IDU	See Hook and Regal (1995), Hickman (2004)
Capture-recapture methods—open populations	Analyses repeat captures/surveys over time (e.g. number of occassions sex workers observed over time, or re-attendances by IDU at injecting room) to estimate total population size and its rate of change over time	See McGeganey (1992)
Truncated Poisson	Takes single data source (e.g. attendances at treatment, arrests, visitis to SEP) and analyses frequency of 1, 2, etc attendances in order to probability of attending once, twice etcc and predict probability and proportion of subjects attending 0 times, and estimate total IDU population.	See Hay (2003)
Enhanced/event Based multipliers	Collects data on event history from multiple data sources/benchmarks (e.g. history of imprisonment, treatment, hostel use), combines them in order to adjust for biases, and combines them with benchmarks to estimate total number of IDU/PDU	See Simeone (1997)
Synthetic estimation	Takes estimates of IDU population in selected sites (usually generated by other indirect methods) and estimates number of IDU in other sites using proportional ratio or regression methods based on single or multiple indicators of IDU that are available in all areas (e.g. number of fatal OD, drug treatment and criminal justice data).	See Rhodes (1993), Frischer (2001)
Back-calculation	Uses information on trends in an observed end-point (e.g. fatal OD), combined with information on the incubation distribution (e.g. heroin/1DU cessation rate, OD and drug related mortality rate) to estimate incidence and prevalence of heroin/1DU use) over time.	See Law (2001), De Angelis (In press)

are no clear sample size calculations that can be made in advance of an analysis that could guarantee a level of reliability. Though as a general rule the greater the amount of data collected and the greater the sampling intensity the better (Wittes 1974). Furthermore, though some methods can generate confidence intervals using standard statistical equations, any uncertainty (or bias) arising from sampling the population is often far outweighed by uncertainty or bias arising from violation of the assumptions and uncertainty surrounding some of the data inputs. It is rarely possible to test empirically whether the final prevalence estimates are true. For this reason it is essential that the estimates are "evidence based" i.e. that the estimates are corroborated or consistent with other information, or other knowledge and expertise is used to help judge whether the estimates are credible. The methods generally used to make indirect prevalence estimates include: multiplier methods, capture-recapture, and others. The following sections discuss each of these methods, offering case studies as examples of their application.

2.1. Multiplier Methods

Multiplier methods (also referred to as ratio-estimation) were probably the first and most common methods for estimating the prevalence of problem drug use. Superficially versatile, easy to use and calculate, in theory they can use any of the data sources given in Table 1. Two elements are required: first, a data source usually called a "benchmark" (representing a known number of problem drug users that have experienced a particular event, such as treatment or arrest or overdose); second, an estimate of the proportion of all problem drug users that have been recorded in the benchmark (e.g. the proportion in treatment might be 1 in 10; or 1 in 50 arrested, or overdose mortality rate amongst problem users might be 1 in 100). The reciprocal of the proportion is termed the multiplier. The benchmark represents the known drug users and the proportion estimates the 'sampling intensity' that generated them. For example, if the benchmark were 3,000 and it was estimated that 20 percent of the population under investigation were recorded on the benchmark, the multiplier would be 5 (since 1/20percent = 5) and the estimated total would be calculated as 15,000 (that is, 5 * 3,000).

In essence, the multiplier is a two-source method (one source is the benchmark, the other is the data used to provide the estimate of the proportion and multiplier). The assumptions of the multiplier method are all those outlined above, i.e., the population of problem drug users needs to be stable and the same during the benchmark recording as during the multiplier estimation; the sample that is used to estimate the multiplier should be representative of the overall population of problem drug users, in practice not easily done; and, it is important that the definition used for the benchmark is precise and matches exactly that used in estimating the multiplier. As an example of this latter point, if arrest data are used for the benchmark then the multiplier needs to find the proportion of drug users arrested,

not those charged or sentenced. Or again, if a number of treatment clinics' records over one year is the benchmark, then the multiplier must relate to attendance at those clinics over that year.

In the 1970s, mortality multipliers were used to estimate the prevalence of opiate use in the United States and United Kingdom (Andima et al., 1973; Hartnoll et al., 1985). For example, Hartnoll et al. (1985) multiplied the annual number of opiate overdose deaths by 50 to 100 on the basis that opiate overdose mortality rate was 1 percent to 2 percent per annum. Multiplier methods also have been applied to arrest data, treatment statistics and HIV reports (see box), and these methods continue to be used (Archibald et al., 2001; Frank et al., 1978; Parker et al., 1988; Godfrey et al., 2002; Dupont, 1973; Hall, 2000).

Various methods have been used to derive the multiplier, all attempting to approximate a random sample of drug users from which to estimate it. These include—not always successfully—site sampling methods (sampling drug users present at a representative set of geographical sites), and 'community sampling' (chain referral or snowball techniques that attempt to produce a representative sample of all drug users).

Nomination also has been used to obtain a multiplier (Parker et al., 1988). This describes a technique where a sample (e.g. injecting drug users) are asked questions about their friends or acquaintances (their nominees) that also are injecting drug users. For example, Parker and colleagues conducted a study with sixty IDU in the Wirral who were asked to nominate their five closest acquaintances and say how many were in treatment last year. The sixty IDU reported 300 other IDU. After removing duplicates this figure was reduced to 170 of whom 55 were identified as being in treatment giving a proportion of 32.4 percent and a multiplier of 3.1 (Parker et al., 1988).

Case Study 1 conducted by Archibald and colleagues (2001) for Toronto used as a benchmark laboratory reports of HIV test results that indicated injecting drug use as a risk factor and a survey of injectors from several Canadian cities asked

Case Study 1. Multiplier Study Based on HIV Tests in Toronto

Benchmark (B)	Number of HIV tests by injecting drug users in 1996—Source: laboratory reports	4050	
Multiplier (M)	Proportion of injectors reporting getting an HIV test in the previous year—Source: community recruited survey of injectors	23% (multiplier = 1/0.23 = 4.35	
Prevalence estimate	B * M (4050*4.35)	17,600	

about being tested for HIV in the same year as the multiplier. In addition to showing how the multiplier method is applied, this example also illustrates the underlying problems with this approach:

- Is the benchmark complete and accurate? It may be necessary to adjust the benchmark, for example, to account for missing exposure information and/or HIV tests.
- Is the multiplier representative of the target population? This presents a greater problem. In this case study information from a community sample of IDUs recruited in a different year and city was used to derive the multiplier. Ideally, the multiplier should be obtained from a representative sample of problem drug users and collected over the time period and place corresponding to the benchmark data. In practice, however, random and representative samples of IDU are nigh on impractical to obtain.

Great caution needs to be exercised when using multiplier studies that are not confirmed, validated, or cross-checked with other information and other studies.

2.2. Capture Recapture

Capture-recapture methods were developed by animal ecologists to estimate animal abundance and the dynamics of animal populations (Begon, 1979). There are two principal types of model: closed and open population models. Open population models relax assumption #1(having a stable population) and because of the need for multiple independent data sets have had limited use in estimating the prevalence of problem drug use (see the two examples below). Closed population models with two data sources are more vulnerable to assumption #4 (having independent data sources) than those with three or more data sources, as it is not possible to test the independence of the two samples in the analysis.

Capture-recapture methods have been used extensively in epidemiology to adjust surveys, surveillance systems, and disease registers for under-ascertainment and therefore to estimate prevalence. (Chandra Sekar et al., 1949; Fienberg, 1992; Hook and Regal, 1995; International Working Group for Disease Monitoring and Forecasting, 1995). Bishop et al (1975) were the first to identify the potential for capture- recapture methods in estimating the prevalence of addiction, which since have been used in many cities worldwide (Hickman et al., 1999, 2004; Hay and McKegany, 1996; Squires et al., 1995; Hay, 2000; Brugha et al., 1998; Domingo-Salvaney et al., 1998, 1995; Bello and Chene, 1997; Kehoe et al., 1992; Comiskey and Barry, 2001; Duque-Portugal et al., 1994; Larson et al., 1994).

Ideally, capture-recapture involves the collection of three or more data sources of problem drug users with sufficient detail on the subjects to identify matches between data sources. Information on the number of matches between the data

		Arrestees with urine positive for opiates (S2)		
		Yes	No	
Methadone	Yes	171	3893	4064
Maintenance (S1)	No	1369	?(x)	
		1540		N

population estimate, N = n_1 , * n_2 / m = 4064 * 1540 / 171 = 36,599 number observed, $n_1 = a + b + c = 171 + 3893 + 1369 = 5433$ hidden, $x_1 = N - n$, or, c * b / a = 36,599 - 5433 or 1369 * 3893 / 171 = 31,16695%c.i. = $1.96 * \sqrt{(n_1, n_2 * b * c)/m^3} = 1.96 * \sqrt{(1540 * 4064 * 3893 * 1369)/171^3} = 4516$ Rounded Estimate of IU in Bangkok in 1991 = 36,600 (32,000 to 40,800)

KEY

a or m = marks, number of people in both S1 and S2

b = number in S1 but not S2

c = number in S2 but not in S1

x = hidden population, number of people not in S1 or S2

 $n_1 = number of people in S1$

 n_2 = number of people in S2

N = total population

sources (i.e., the number of people that occur in more than one data source) is used to estimate the sampling intensity (i.e., the total proportion of injectors in the samples). These estimates of the number unobserved are then combined with the number in the data sources to generate the overall prevalence estimate. Studies with two samples can be easily calculated (see below). Those with three, four or more samples require statistical packages (such as STATA or GLIM or SPSS) as the data are analyzed using log-linear models with dependencies (technically, 'interactions') between data sources to generate an adjusted prevalence estimate. The following references give an essential background to the methods and their use in epidemiology (Hook and Regal, 1995; International Working Group for Disease Monitoring and Forecasting, 1995).

Case study 2a shows an example by Mastro and colleagues (1994) who carried out a two sample study in Bangkok in 1991. They collected two samples, 4064 heroin users in methadone treatment and 1540 people that had been arrested and tested positive for opiates. There were 171 people on both lists giving an estimate of 36,600 opiate users (0.5 percent of total population) in Bangkok in 1991.

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Case Study 2b. Multi-data source Capture-recapture Study of Prevalence of IDU in Brighton, UK, 2001

Bright	on	Treatment							
			Y	Yes			No		
					Arrest	Referral			
		Yes		No	3	Yes		No	
					Survey	& A&E			
		Yes	No	Yes	No	Yes	No	Yes	No
Syringe	Yes	1	8	7	65	3	19	36	521
Exchange	No	2	7	6	103	2	42	74	

Data sources:

Specialist							
Drug	Arrest	Survey &	, ,	Total	Total		
Treatment	Referral	A&E	Exchange	records	Individuals	Matched	
199	84	131	660	1074	896	156	17%

Prevalence estimate:							
population		estimate of					
(15-44)	observed	unobserved	Total nun	nber IDU (95% CI)	Prevalence (95% CI)		
117,032	896	1,408	2,304	1514-3737	2.0% 1.3-3.2%		

Model Selection:

Interactions: treatment*arrest referral, treatment *syringe exchange, arrest referral*survey_a&e syringe exchange*survey_a&e G^2 11.81, p-value 0.98, degrees of freedom 24

The problem with the two-sample study is that it is not known whether the two data sources (police and treatment) are independent (assumption #4). If not, and the proportion of the population captured or observed in the data sources is low (1 in 7 in the Bangkok study) then the potential for error is large (Wittes et al., 1974).

In a study in Brighton four data sources were analyzed (specialist drug treatment, criminal justice, syringe exchange, and community survey). The box (above) shows the contingency table, summary of the data sources, prevalence estimates and the best fitting model. The contingency table, instead of a 2 *2 as in the Bangkok study, shows the number of subjects across all four data sources. The number unobserved in the last cell with a "." represents those cases that do not appear on any of the data sources. In total 156 subjects (17 percent) were on more than one data source and one person was on all four data sources. The analysis suggested that the best model identified complex interactions between the data sources, making the basic analyses difficult and less reliable than if only a simple model was required for the data. The prevalence estimate itself could be considered high at 2 percent among adults aged 15–44. The authors note that compared to many capture-recapture studies for drug use the estimated number and proportion of

unobserved subjects is comparatively low (i.e., \sim 900 : 1400, 1 : 1.5); that the capture-recapture estimate was lower than for a mortality multiplier estimate; and that local policy-makers were consulted and agreed that the estimate was consistent with other available information.

We should note here that complex dependency models can result from heterogeneity among the subjects (violation of assumption #2). Heterogeneity is often regarded as inevitable when using health data (Hook and Regal, 1995) as there are many examples of differences in health seeking behaviors and arrests by gender, age-group, social class, ethnic group, and degree of dependence. To avoid or limit the influence of these factors, analyses are made by first stratifying the data into more homogeneous subsets of people that are analyzed separately (for example, fitting separate models for males and females or by age group). Alternatively, covariate capture-recapture techniques have been developed that allow fewer models to be fitted including both dependencies between data sources and those potentially between covariates (e.g., by gender and age-group) (Tilling and Sterne, 1999).

Two other assumptions that were potentially violated in this and many capture-recapture studies are *misclassification* bias (assumption #3) and closed population (assumption #1). Often there is insufficient information in the data sources to identify matching individuals; moreover subjects may give pseudonyms to different data sources to protect their identity. Studies would benefit by estimating the misclassification error thus allowing sensitivity tests of the robustness of the estimates (as animal ecology studies allow for loss of marks).

A closed population (i.e., no deaths, new cases, cessation or migration) is clearly an impossibility, but the bias of using an open capture-recapture method can be limited if the study time interval is short in comparison to the life cycle of the subject (e.g., a year for an injecting drug user may not be too serious a bias and allows sufficient data to be gathered to identify matches). Alternatively, open capture-recapture models seek to estimate population prevalence and change over time. However, there are very few examples of this approach in the epidemiological literature. One such study estimated the prevalence of street sex workers in Glasgow (McKeganey et al., 1992) through fieldwork over a succession of nights. They built "capture-histories" of women (e.g., on how many nights they were observed). The study suggested that the number of sex workers on the street remained approximately the same over a year but that the population of sex workers changed at approximately 8 percent per week. A new study by Kimber and colleagues used attendance histories at a safe injecting room to estimate prevalence over time (Jo Kimber, personal communication). This type of application is rare as there are hardly any single data sources that could meet assumption #2, requiring the data source to be representative of the target population. Pollack (1990) proposed mixed closed and open models as an answer to problems of heterogeneity, dependence, and dynamic populations, which may prove interesting to pilot in drug abuse.

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2.3. Other Indirect Methods

Multiplier and capture-recapture estimates are the most common indirect prevalence methods used for problem drug use. Below, we mention other methods, some more recent in their development: truncated poisson, synthetic estimation, back calculation, and enhanced/event based multipliers.

2.3.1. Truncated Poisson

Truncated Poisson methods use information on repeat events to estimate the size of the population with 0 events. All the assumptions above apply, however, the strength of two of these assumptions and the availability of data limit its use. For instance, the assumption that repeat events are independent, i.e., that a person arrested or in treatment once is as likely to be re-arrested or re-enter treatment as someone who has not yet been "captured"; and the assumption that *all* subjects are as likely as each other to generate an event are easily violated. Also, as in the case of open capture-recapture models, the problem is to find a single data source that is representative of problem drug users. Certainly, criminal justice or specialist drug treatment data alone are not sufficient. Hay and Smit (2003) demonstrated the potential of truncated poisson applied to injecting drug users attending a syringe exchange in Scotland, estimating from attendance records of 647 subjects in a city in Scotland that there were a total of 1041 injectors.

2.3.2. Synthetic Estimation

Synthetic estimation or the multiple indicator method is a form of extrapolation (or technically 'regression on principal components'), which makes use of known prevalence figures in certain regions (that may have been estimated using multiplier or capture-recapture methods) to estimate prevalence in other regions. To do this correctly, these regions for which prevalence is being estimated must have data sources that are the same as (or very similar to) the regions for which prevalence estimates exist.

Extrapolation can be based on a single value, e.g., the proportion of opiate overdose deaths (Hall et al., 2000), or multiple indicators (Frischer 2001, Kraus 2003). It should be noted that there are some technical and statistical considerations that apply when more than one anchor point is used in a regression analysis, requiring discussion with an experienced statistician. For example, should a Poisson regression be used as opposed to using simple linear regression analysis and should rates or log-transformed data be used; should a weighting for the different anchor points be established to represent the reliability of the problem drug use prevalence estimate; and is the relationship between the drug indicator and the problem

drug use prevalence rates similar across all the data points and is the relationship between prevalence and indicators valid.

2.3.3. Back-calculation

Law and colleagues (2001), and De Angelis and colleagues (in press) adapted back-calculation methods to estimate the incidence and prevalence of heroin use. The back-calculation method developed in AIDS epidemiology is based on the relationship between the time of infection (the presence of HIV), the incubation time, and the development of the disease (the diagnosis of AIDS). Knowledge of any two of these three components allows estimation of the third. Typically, the distribution of the incubation time and the incidence of the end point are assumed known and the infection process underlying the observed incidence is estimated. The estimated infection process is then used with the same information on the incubation time to predict the incidence and prevalence of the end-point of interest. When used for drug abuse epidemiology the observed incidence of the end-point has generally been opiate overdose death, with trends over time provided by routine mortality statistics. The "incubation" distribution is the distribution of the time between starting and stopping injecting, where the stopping process is the result of either a fatal overdose or the actual cessation of injecting. The data demands are considerable including reliable mortality statistics to identify the number of opiate overdose deaths, data on the opiate overdose and other drug related mortality rates of injecting drug users, and information on the cessation rates from injecting.

2.3.4. Enhanced/Event Based Multipliers

Simeone and colleagues (1997) have suggested modifications to the simple multiplier. Instead of a single proportion as a multiplier, a detailed multiple event history using multiple data sources are collected, in order theoretically to adjust for the inherent biases present in any single data source. However, these methods have only been piloted and are not in general use.

3. CONCLUSIONS

This chapter presented the indirect methods currently being used to estimate the prevalence of drug abuse in various populations. We have been critical of these methods pointing out their limitations and that the estimates derived from them need to be interpreted with caution. However, we believe that they are the answer to the problem of estimating the prevalence of rare problem drug using behaviors such as the use of heroin, drug injecting, or crack-cocaine use as population

surveys are inefficient and not cost effective. Data sources for capture-recapture and multplier estimates should be carefully chosen to minimize both dependence and heterogeneity. Most communities have data that are available and these can be assessed for their utility for prevalence estimation. For example, do the data sources collect data on drug profile (injecting status, and problem drugs), collect identifiers to allow matching with other data sources /or/ if anonymised suffer little under-reporting; would problem drug users remember or recognise being captured by the data source, are only a sub-set of problem drug users captured by the data source; is it known how the data sources relate to other potential data sources. If the available data sources are poor—recommend steps to policy-makers (and data owners) to improve them for future estimation work. Collecting the data is the most time consuming part of prevalence estimation work. This work could be dramatically reduced if contributing to prevalence estimates was one of the objectives of routine data on problem drug use—such that a "public health surveillance" system of problem drug use was developed that specifically linked and integrated multiple data sources to allow prevalence estimation.

Finally, multiplier and capture-recapture estimation methods tend to be more reliable within discrete geographical locations in part to avoid heterogeneity (i.e., the relationship between the population of problem drug users and data sources is likely to vary from city to city), which has implications for public health surveillance and the design of studies.

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